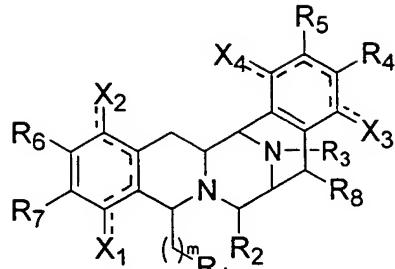


CLAIMS

3 1. A compound having the structure (I):



(1)

8 wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic,
9 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
10 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently
11 hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
12 moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or
13 cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-$
14 SR_D , $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
15 occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
16 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
17 moiety:

18 wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-$
19 SOR_E , $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
20 moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an
21 aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio,
22 heteroaryloxy, or heteroarylthio moiety;

23 wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an
24 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is
25 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
26 alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

1 wherein R₄ and R₆ are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl, 2 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

3 wherein R₅ and R₇ are each independently hydrogen, -OR_G, -C(=O)R_G, -CO₂R_G, -CN, - 4 SCN, halogen, -SR_G, -SOR_G, -SO₂R_G, -NO₂, -N(R_G)₂, -NHC(O)R_G, or an aliphatic, 5 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently 6 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, 7 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

8 wherein R₈ is hydrogen, alkyl, -OH, protected hydroxyl, =O, -CN, -SCN, halogen, -SH, 9 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

10 wherein m is 0-5;

11 wherein X₁, X₂, X₃ and X₄ are each independently hydrogen, -OR_H, =O, -C(=O)R_H, 12 -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an 13 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is 14 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, 15 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

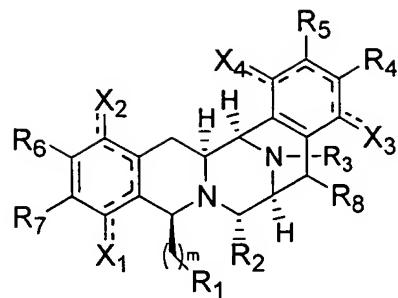
16 whereby if at least either X₁ and X₂ or X₃ and X₄ are doubly bonded to the 6-membered 17 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds 18 and one double bond, and a quinone moiety is generated, or if at least either X₁ and X₂ or X₃ and 19 X₄ are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6- 20 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is 21 generated;

22 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may 23 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and 24 each of the foregoing aryl or heteroaryl moieties may independently be substituted or 25 unsubstituted; and

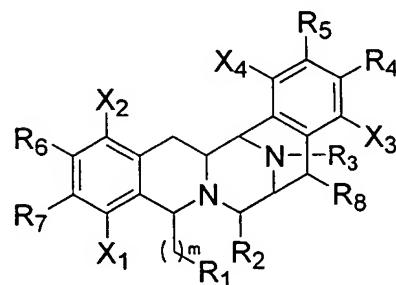
26 pharmaceutically acceptable derivatives thereof.

27

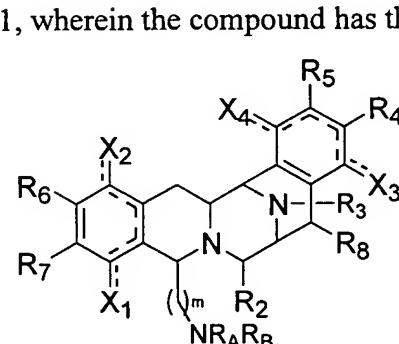
28 2. The compound of claim 1, wherein the compound has the stereochemistry and structure 29 of formula (Ia):



(Ia)



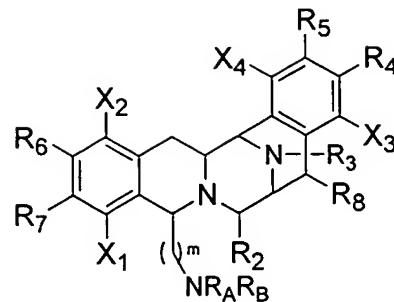
(II)



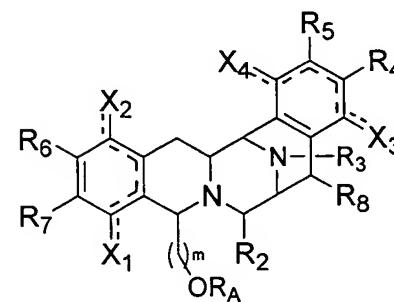
(III)

4. The compound of claim 1, wherein the compound has the structure (III):

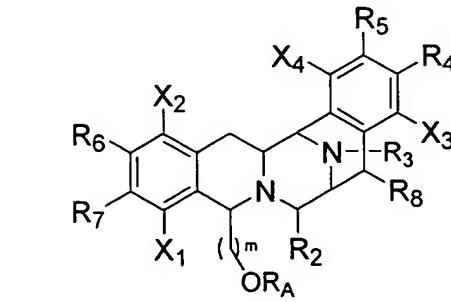
5. The compound of claim 1, wherein the compound has the structure (IV):



(IV)

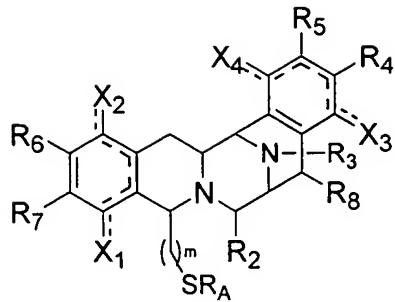


(V)

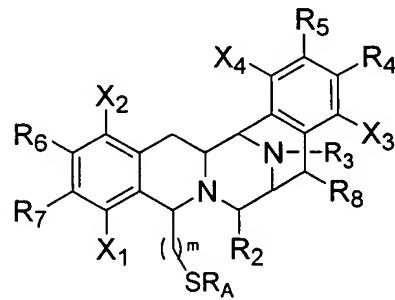


(VI)

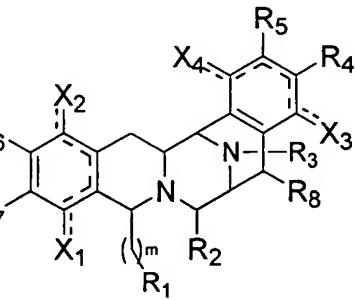
8. The compound of claim 1, wherein the compound has the general structure (VII):



(VII)



(VIII)



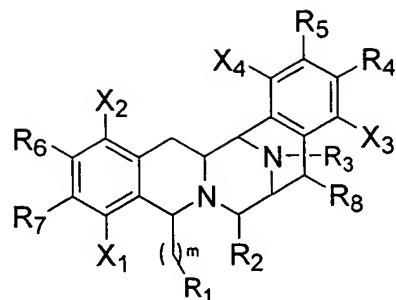
(IX)

wherein R1 is a substituted or unsubstituted, cyclic or acyclic, branched or unbranched

aliphatic or heteroaliphatic moiety, or is a substituted or unsubstituted aryl or heteroaryl moiety.

16

17 11. The compound of claim 1, wherein the compound has the general structure (X):



(X)

5 wherein R₁ is a substituted or unsubstituted, cyclic or acyclic, branched or unbranched
 6 aliphatic or heteroaliphatic moiety, or is a substituted or unsubstituted aryl or heteroaryl moiety.

8 12. The compound of claim 1, having one or more of the following limitations:

9 when m is 1, R₁ excludes any one or more of the following groups: -NH(protecting
 10 group), -NH₂, -NHCOCOMe, -NHCOC(Me)(OMe)(OMe), -NHCOCH(NH₂)CH₃, -
 11 NHCOCH(NH(acyl))CH₃ -NHCOCH(NH₂)Ac, or NHCOCH(NHCOOBn)(Me); -
 12 O(C=O)C(CH₃)=C(CH₃)H; -OH, -O(protecting group), -O(COCH₃), -O(C=O)CH₂CH₃; or

13 when m is 1; when X₁, X₂, X₃ and X₄ are each =O; when R₂ is -CN or -OH; when R₄ and
 14 R₆ are each -CH₃; when R₅ and R₇ are each -OCH₃; when R₈ is H; and R₁ is -NH(C=O)R_C, then
 15 R_C is not -CH(NR_WR_Y)(CH₂R_Z) where R_W and R_Y are each independently hydrogen or C₁₋₇
 16 alkyl, aryl(C₁₋₄)alkyl, (C₁₋₄)alkylaryl, a substituted sulfonyl (-S(O)₂-) group, or a substituted acyl
 17 group, and where R_Z is hydrogen or C₁₋₄ alkyl; or

18 when m is 1; when X₁, X₂, X₃ and X₄ are each =O; when R₂ is -CN; when R₄ and R₆ are
 19 each -CH₃; when R₅ and R₇ are each -OCH₃; when R₈ is H; and R₁ is -NH(C=O)R_C, then R_C is
 20 not -C(OH)(Me)CH₂(C=O)Me; or

21 when m is 1 and when R₂ is H; and R₁ is -NH(C=O)R_C, then R_C is not -
 22 CH(Me)NH(C=O)O(CH₂)Ph; or

23 when m is 0; R₂ is H; X₃ is H; and R₁ is -C(=O)R_A, then R_A is not -O(alkyl); or

24 when R₂ is H; m is 1; and R₁ is -OR_A, then R_A is not -C(=O)R_C, or S(O)₂R_C, wherein R_C
 25 is an alkyl moiety.

1 13. The compound of claim 1, wherein m is 0 or 1.
2
3 14. The compound of claim 1, wherein R₂ is CN, -SCN, =O, OH, protected hydroxyl, H, or
4 alkoxy.
5
6 15. The compound of claim 1, wherein R₂ is hydrogen, hydroxyl, -CN or -SCN.
7
8 16. The compound of claim 1, wherein R₈ is hydrogen.
9
10 17. The compound of claim 1, wherein X₁, X₂, X₃, and X₄ are each independently alkoxy,
11 OH, protected hydroxyl, or =O.
12
13 18. The compound of claim 1, wherein R₂ is CN, -SCN, =O, OH, protected hydroxyl, H, or
14 alkoxy; R₃ is hydrogen, a nitrogen protecting group, -CN, aliphatic, or aryl; R₄ and R₆ are each
15 alkyl; R₅ and R₇ are each alkyloxy or thioalkyl; R₈ is hydrogen, alkyl, -OH, protected hydroxyl,
16 =O, CN, halogen, SH, alkoxy, thioalkyl, amino, or alkylamino; and X₁, X₂, X₃, and X₄ are each
17 independently alkoxy, OH or =O.
18
19 19. The compound of claim 1, wherein R₂ is -CN, -SCN, -OH, protected hydroxyl, H, or
20 alkoxy; R₃ is hydrogen, a nitrogen protecting group, aliphatic, or aryl; R₄ and R₆ are each alkyl;
21 R₅ and R₇ are each alkyloxy or thioalkyl; X₁ and X₄ are each -OH; R₈ is hydrogen, alkyl, OH,
22 protected hydroxyl, =O, CN, halogen, SH, alkoxy, thioalkyl, amino, or alkylamino; and X₂ and
23 X₃ are each alkyloxy or thioalkyl.
24
25 20. The compound of claim 1, wherein X₁ is OH, X₂ is OCH₃, X₃ is OCH₃, X₄ is OH, R₂ is
26 CN, H or OH, R₃ is Me, R₄ is CH₃, R₅ is OCH₃, R₆ is CH₃, R₇ is OCH₃, and R₈ is H.
27
28 21. The compound of claim 1, wherein R₁ is OR_A, SR_A, or NR_AR_B, wherein R_A and R_B are
29 each independently hydrogen, -(C=O)R_C or an aliphatic, heteroaliphatic, aryl, or heteroaryl
30 moiety, wherein R_C is -(C=O)R_D, or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety, and

1 wherein R_D is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or wherein R_A and R_B ,
2 taken together, form a heterocyclic moiety,

3 whereby each of said aliphatic and heteroaliphatic moieties is independently
4 substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of said aryl,
5 heteroaryl and heterocyclic moieties is independently substituted or unsubstituted.

6

7 22. The compound of claim 1, wherein R_1 is OR_A , SR_A , or NR_AR_B , wherein R_A and R_B are
8 each independently hydrogen, $-(C=O)R_C$, or an aryl, (aliphatic)aryl, (heteroaliphatic)aryl,
9 heteroaryl, (aliphatic)heteroaryl, or (heteroaliphatic)heteroaryl moiety, wherein R_C is an aryl,
10 (aliphatic)aryl, (heteroaliphatic)aryl, heteroaryl, (aliphatic)heteroaryl, or
11 (heteroaliphatic)heteroaryl moiety, or wherein R_A and R_B taken together form a heterocyclic
12 moiety,

13 whereby each of said aliphatic and heteroaliphatic moieties is independently substituted
14 or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of said aryl, heteroaryl
15 and heterocyclic moieties is independently substituted or unsubstituted.

16

17 23. The compound of claim 1, wherein R_1 is $-NR_AC(=O)R_C$, wherein R_A is hydrogen or
18 lower alkyl, and R_C is a substituted or unsubstituted, branched or unbranched, cyclic or acyclic
19 aliphatic or heteroaliphatic moiety, or a substituted or unsubstituted aryl or heteroaryl moiety, or
20 wherein R_A and R_C taken together form a heterocyclic or heteroaryl moiety.

21

22 24. The compound of claim 1, wherein R_1 is $NR_AC(=O)R_C$, wherein R_A is hydrogen or lower
23 alkyl, and R_C is an aryl, (aliphatic)aryl, (aliphatic)heteroaryl, heteroaryl, (heteroaliphatic)aryl, or
24 (heteroaliphatic)heteroaryl moiety, or wherein R_A and R_C taken together form a heterocyclic or
25 heteroaryl moiety;

26 whereby each of said aliphatic and heteroaliphatic moieties is independently
27 substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of
28 said aryl, heteroaryl and heterocyclic moieties is independently substituted or
29 unsubstituted.

30

1 25. The compound of claim 1, wherein R_1 is a substituted or unsubstituted, branched or
2 unbranched, cyclic or acyclic aliphatic or heteroaliphatic moiety, or a substituted or unsubstituted
3 aryl or heteroaryl moiety.

4

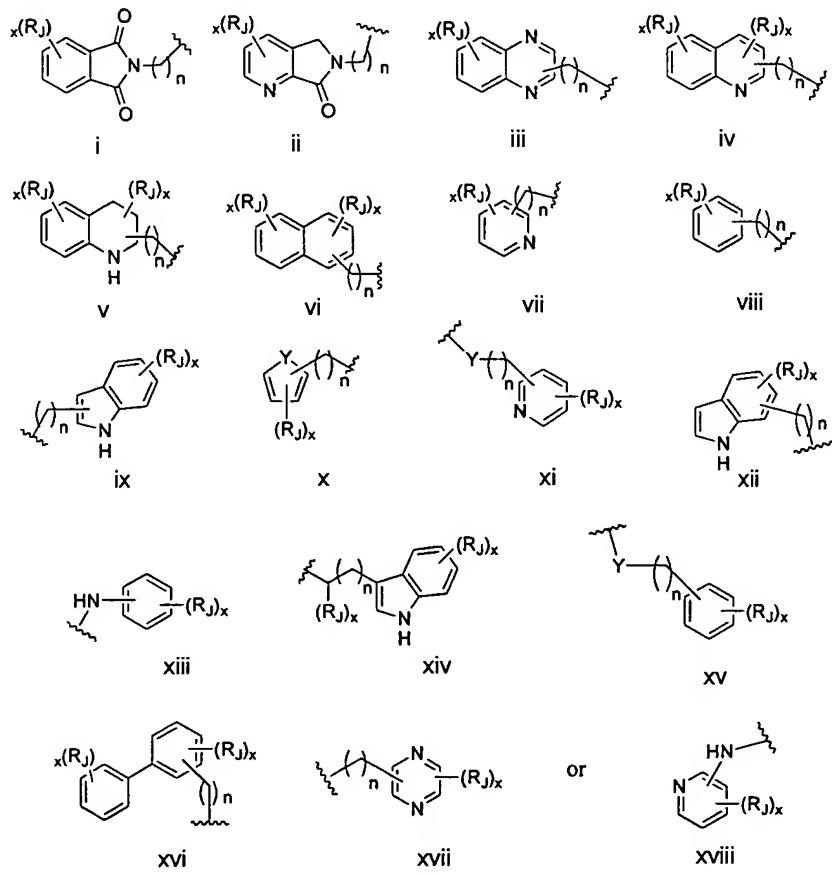
5 26. The compound of claim 1, wherein R_1 is an aryl, (aliphatic)aryl, (aliphatic)heteroaryl,
6 heteroaryl, (heteroaliphatic)aryl, or (heteroaliphatic)heteroaryl moiety;

7 whereby each of said aliphatic and heteroaliphatic moieties is independently
8 substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of
9 said aryl, heteroaryl and heterocyclic moieties is independently substituted or
10 unsubstituted;

11

12 27. The compound of claim 1, wherein any one or more of R_1 , R_A , R_B , R_C , or R_D is
13 independently any one of the following groups:

14



15

16

1 wherein each occurrence of R_J is independently hydrogen, a protecting group, $-OR_K$, $=O$,
2 $-C(=O)R_K$, $-CO_2R_K$, $-CN$, $-SCN$, halogen, $-SR_K$, $-SOR_K$, $-SO_2R_K$, $-NO_2$, $-N(R_K)_2$, $-NHC(O)R_K$,
3 $-B(OR_K)_2$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of
4 R_K is independently hydrogen, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or
5 wherein two occurrences of R_K , taken together form a cyclic aliphatic or heteroaliphatic moiety;
6 wherein each occurrence of Y is independently O, S or NH; wherein each occurrence of x is
7 independently 0-5; and wherein each occurrence of n is independently 0-3, or wherein R_J is a
8 labeling reagent,

9 whereby each of said aliphatic and heteroaliphatic moieties are independently substituted
10 or unsubstituted, branched or unbranched or cyclic or acyclic, and each of said aryl and
11 heteroaryl moieties is independently substituted or unsubstituted.

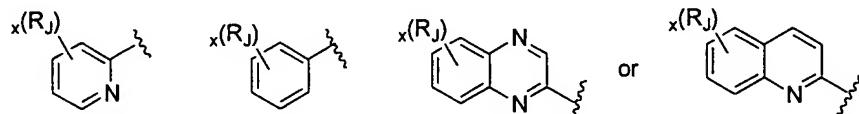
12

13 28. The compound of claim 27, wherein R_1 is NR_AR_B , R_A is hydrogen, R_B is $-(C=O)R_C$, and
14 R_C is iii, iv, vii, viii, ix, x, xv, or xvii, or R_A and R_C taken together form the structure of i or ii.

15

16

17 29. The compound of claim 27, wherein R_1 is NR_AR_B and R_A is hydrogen, R_B is $-(C=O)R_C$,
18 and R_C is



22 30. The compound of claim 27, 28 or 29, wherein R_J is hydrogen, halogen, $-OH$, lower alkyl
23 or lower alkoxy.

24

25 31. The compound of claim 27, 28 or 29, wherein R_J is a linker-biotin or a linker-fluorescein
26 moiety.

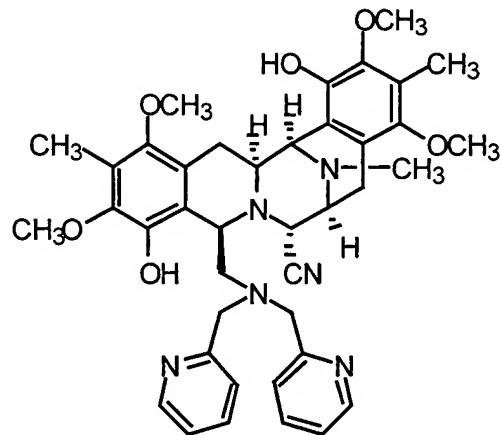
27

28 32. The compound of claim 27, 28 or 29, wherein x is 1 or 2.

29

1 33. The compound of claim 1, wherein the compound has the structure:

2

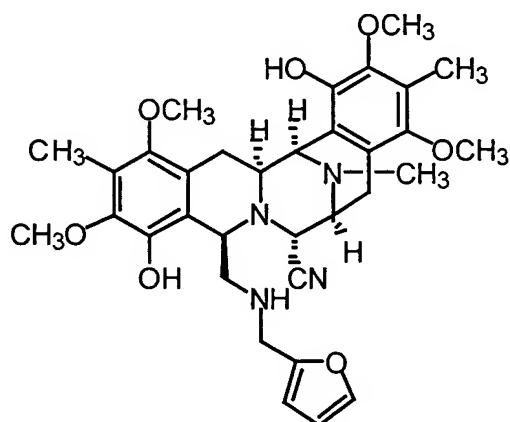


3

4

5 34. The compound of claim 1, wherein said compound has the structure:

6

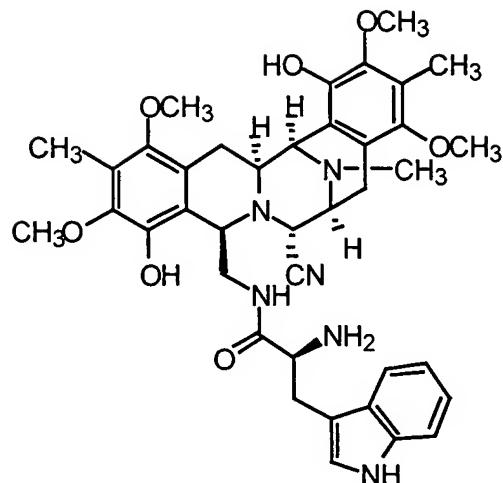


7

8

9 35. The compound of claim 1, wherein the compound has the structure:

10

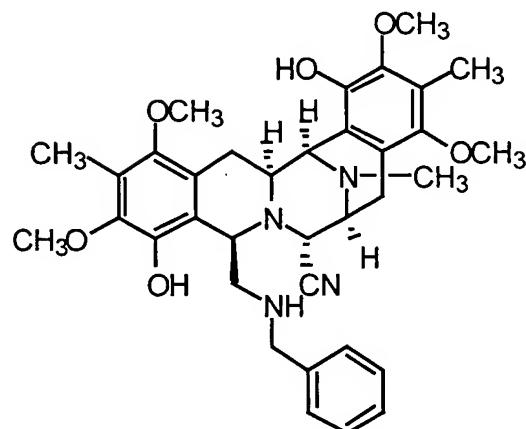


1

2

3 36. The compound of claim 1, wherein the compound has the structure:

4

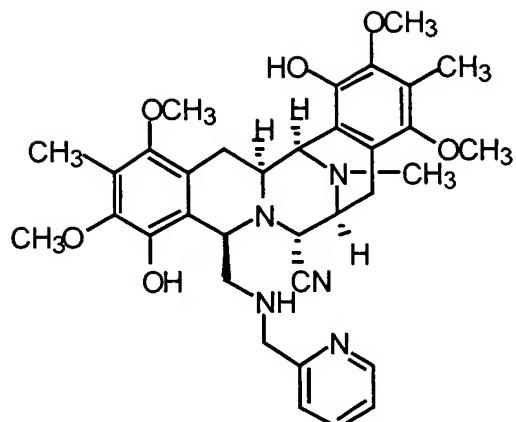


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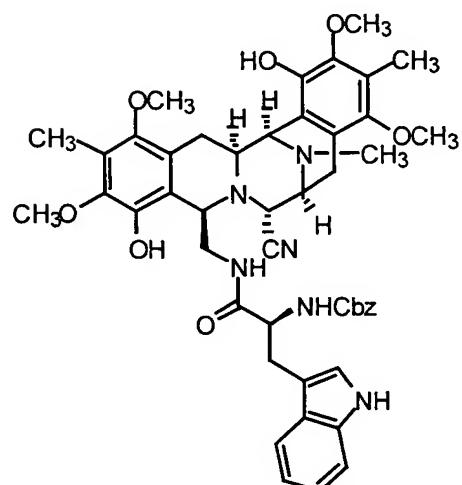
6

7 37. The compound of claim 1, wherein the compound has the structure:

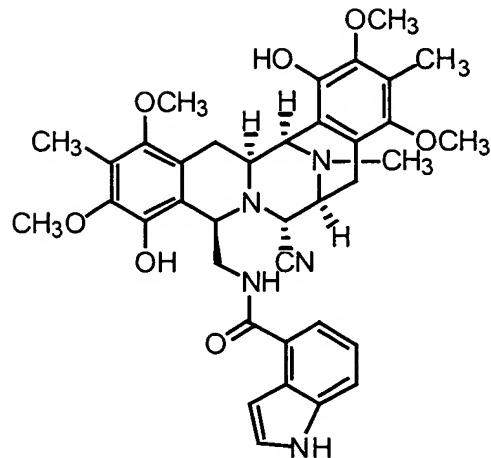
8



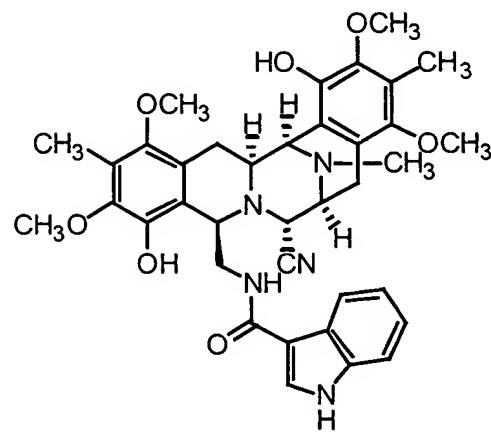
1
2
3
4 38. The compound of claim 1, wherein said compound has the structure:



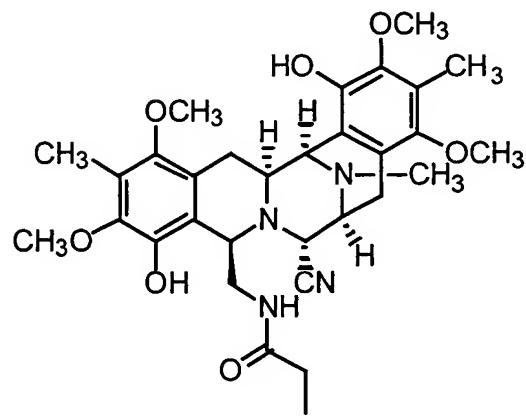
5
6
7
8 39. The compound of claim 1, wherein the compound has the structure:



1
2
3 40. The compound of claim 1, wherein the compound has the structure:
4



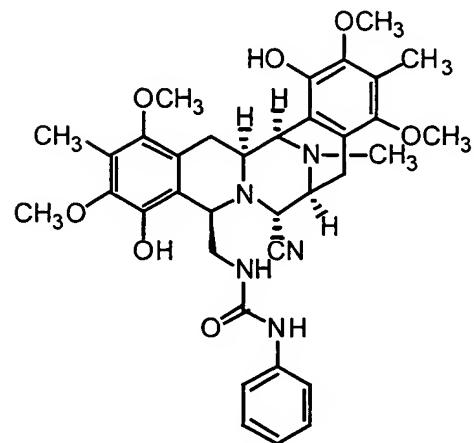
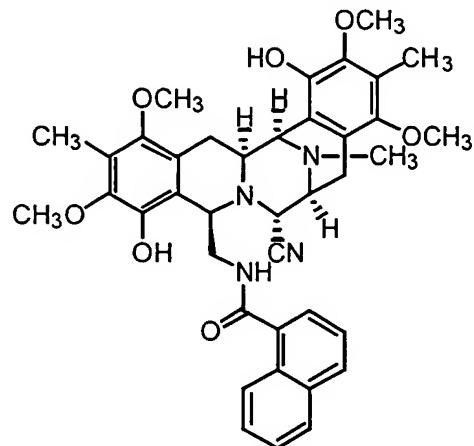
5
6
7 41. The compound of claim 1, wherein the compound has the structure:
8

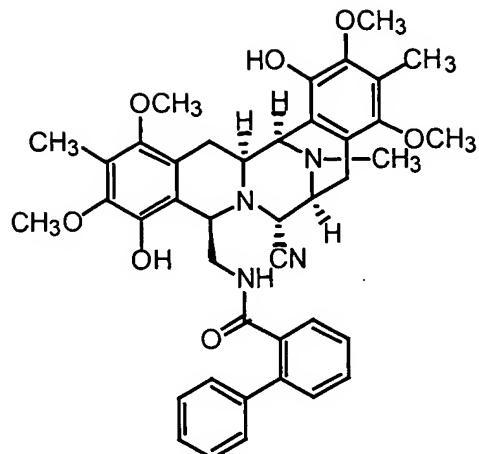


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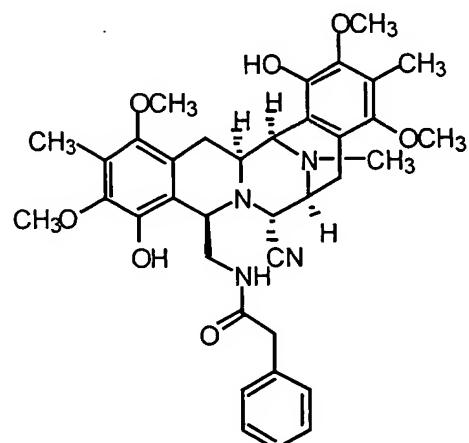
1 42. The compound of claim 1, wherein the compound has the structure:

2

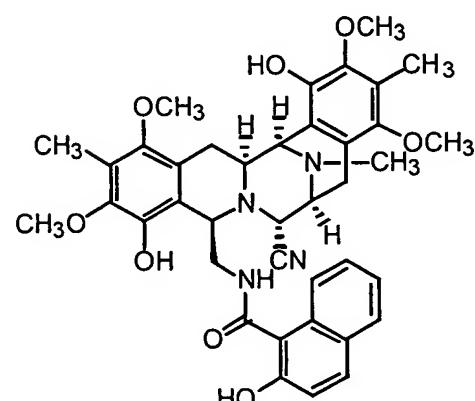




45. The compound of claim 1, wherein the compound has the structure:

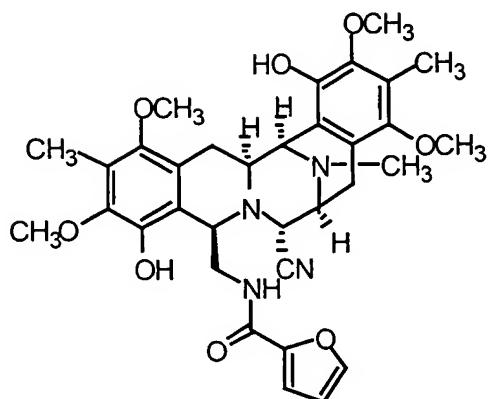


46. The compound of claim 1, wherein the compound has the structure:



1 47. The compound of claim 1, wherein the compound has the structure:

2

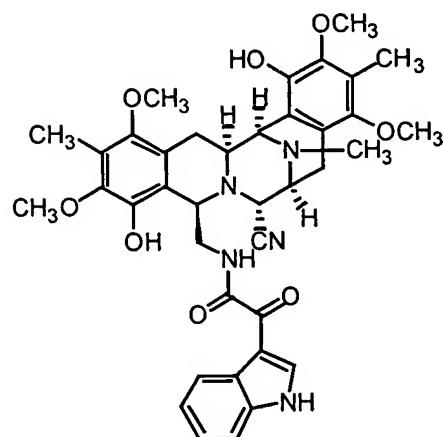


3

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5 48. The compound of claim 1, wherein the compound has the structure:

6

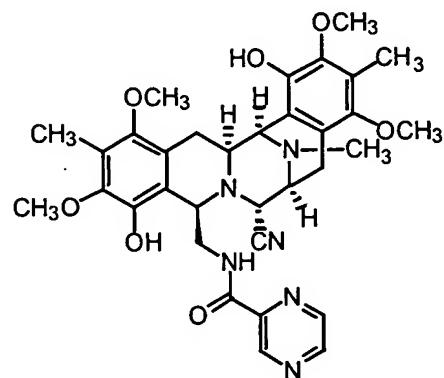


7

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9 49. The compound of claim 1, wherein the compound has the structure:

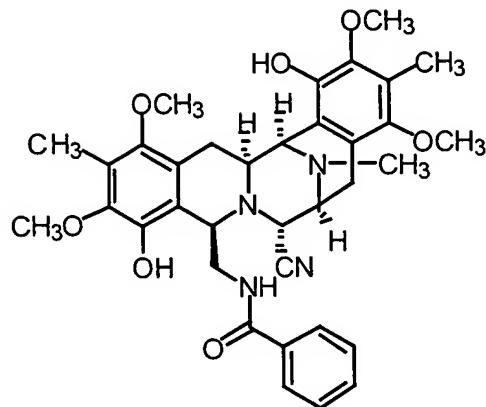
10



11

1 50. The compound of claim 1, wherein the compound has the structure:

2



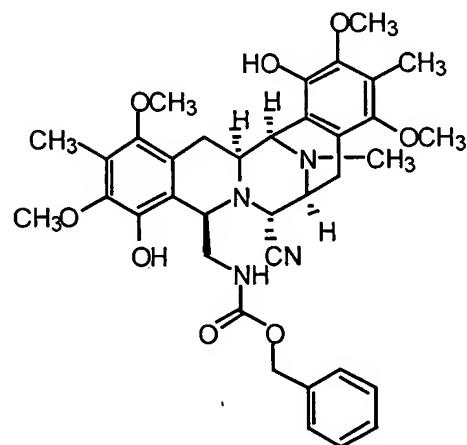
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5

6 51. The compound of claim 1, wherein the compound has the structure:

7

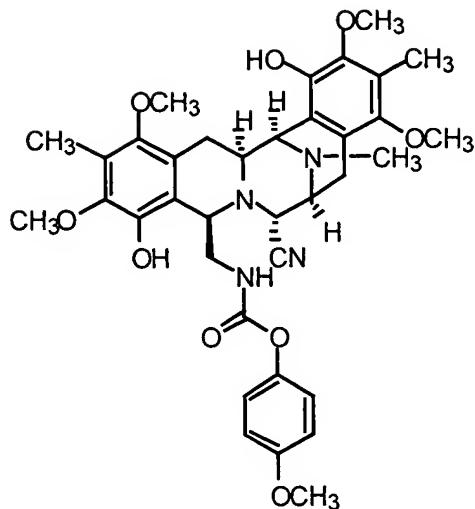


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9

10 52. The compound of claim 1, wherein the compound has the structure:

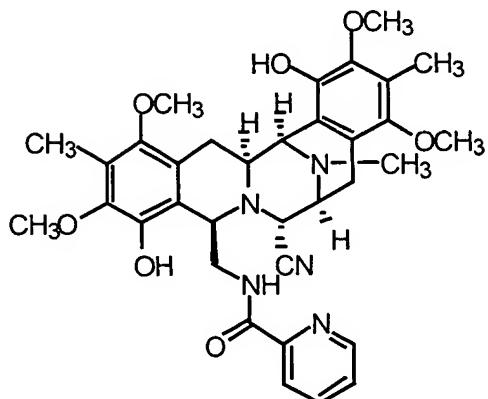
11



1

2

3 53. The compound of claim 1, wherein the compound has the structure:

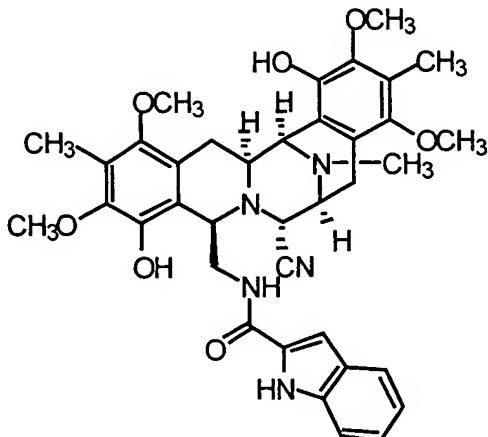


4

5

6 54. The compound of claim 1, wherein the compound has the structure:

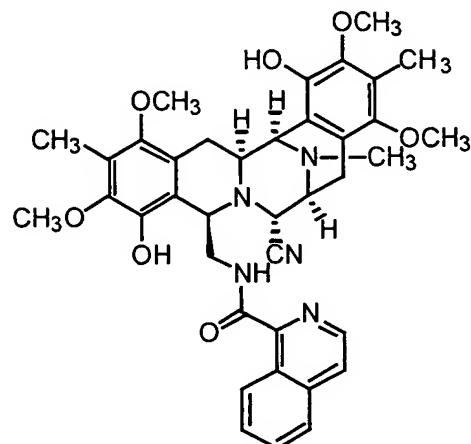
7



8

1 55. The compound of claim 1, wherein the compound has the structure:

2

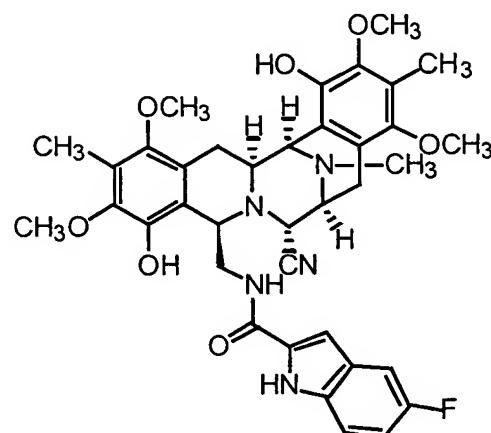


3

4

5 56. The compound of claim 1, wherein the compound has the structure:

6

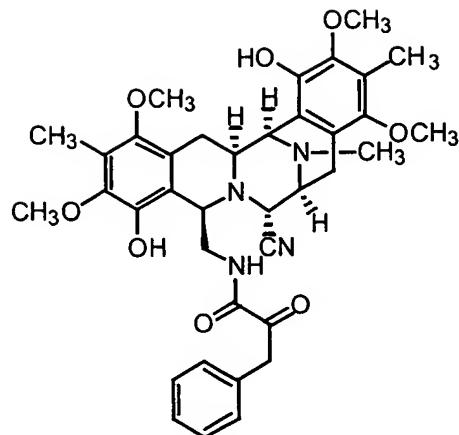


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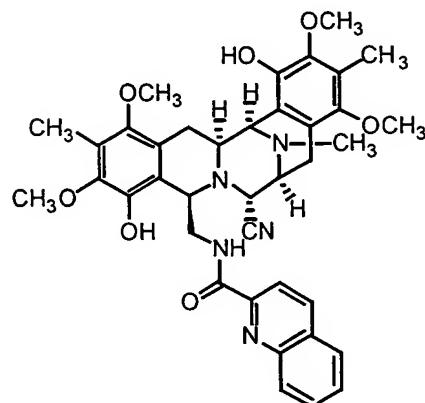
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9 57. The compound of claim 1, wherein the compound has the structure:

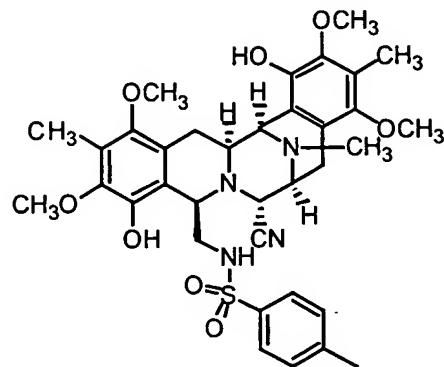
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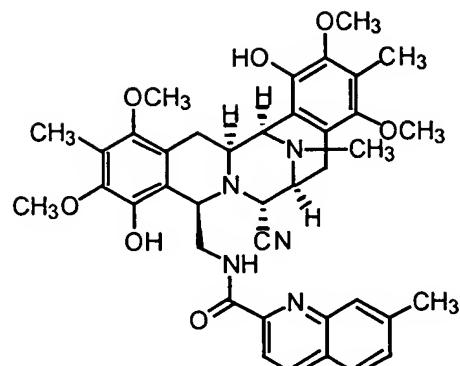
1
2
3 58. The compound of claim 1, wherein the compound has the structure:



4
5
6
7 59. The compound of claim 1, wherein the compound has the structure:



8
9
10
11 60. The compound of claim 1, wherein the compound has the structure:

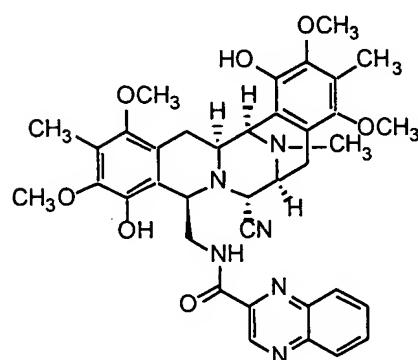


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2

3 61. The compound of claim 1, wherein the compound has the structure:

4

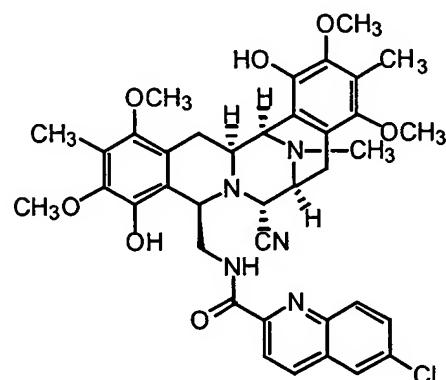


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7 62. The compound of claim 1, wherein the compound has the structure:

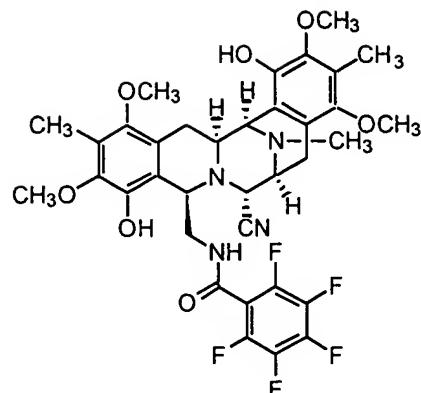
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9

10 63. The compound of claim 1, wherein the compound has the structure:

11



1

2

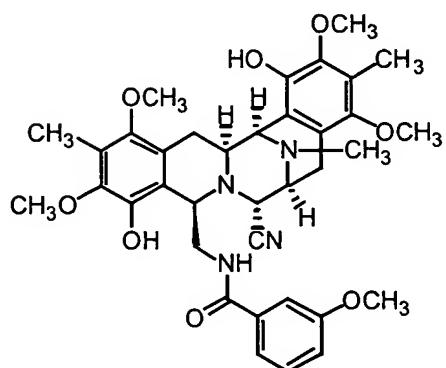
3 64. The compound of claim 1, wherein the compound has the structure:

4

5

6

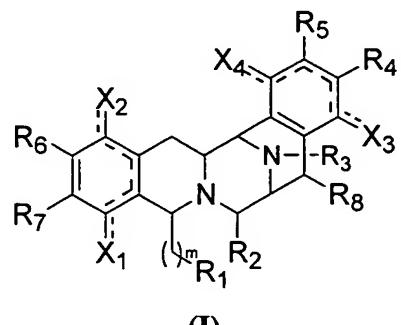
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8

9

10 65. A pharmaceutical composition comprising
11 a compound having the structure (I)



12

13

14

1 wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic,
2 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
3 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently
4 hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
5 moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or
6 cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-$
7 SR_D , $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
8 occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
9 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
10 moiety;

11 wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-$
12 SOR_E , $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
13 moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an
14 aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio,
15 heteroaryloxy, or heteroarylthio moiety;

16 wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an
17 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is
18 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
19 alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

20 wherein R_4 and R_6 are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl,
21 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

22 wherein R_5 and R_7 are each independently hydrogen, $-OR_G$, $-C(=O)R_G$, $-CO_2R_G$, $-CN$, $-$
23 SCN , halogen, $-SR_G$, $-SOR_G$, $-SO_2R_G$, $-NO_2$, $-N(R_G)_2$, $-NHC(O)R_G$, or an aliphatic,
24 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently
25 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
26 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

27 wherein R_8 is hydrogen, alkyl, $-OH$, protected hydroxyl, $=O$, $-CN$, $-SCN$, halogen, $-SH$,
28 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

29 wherein m is 0-5;

30 wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, $-OR_H$, $=O$, $-C(=O)R_H$,

1 -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an
2 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
3 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
4 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

5 whereby if at least either X₁ and X₂ or X₃ and X₄ are doubly bonded to the 6-membered
6 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
7 and one double bond, and a quinone moiety is generated, or if at least either X₁ and X₂ or X₃ and
8 X₄ are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
9 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
10 generated;

11 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
12 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
13 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
14 unsubstituted, and pharmaceutically acceptable derivatives thereof; and

15 a pharmaceutically acceptable carrier or diluent.

16

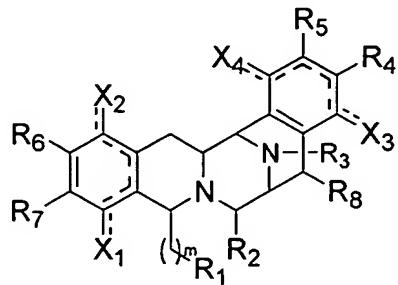
17 66. The pharmaceutical composition of claim 65, wherein the pharmaceutical composition
18 optionally further comprises one or more additional therapeutic agents.

19

20 67. The pharmaceutical composition of claim 66, wherein said composition further comprises
21 one or more cytotoxic agents.

22

23 68. A method for inhibiting the growth of or killing cancer cells comprising:
24 contacting the cells with an amount of a composition effective to inhibit the growth of or
25 to kill cancer cells, the composition comprising a compound of formula (I) or pharmaceutically
26 derivatives thereof:



27

1 (I)
2

3 wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic,
4 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
5 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently
6 hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
7 moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or
8 cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-$
9 SR_D , $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
10 occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
11 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
12 moiety;

13 wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-$
14 SOR_E , $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
15 moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an
16 aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio,
17 heteroaryloxy, or heteroarylthio moiety;

18 wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an
19 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is
20 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
21 alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

22 wherein R_4 and R_6 are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl,
23 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

24 wherein R_5 and R_7 are each independently hydrogen, $-OR_G$, $-C(=O)R_G$, $-CO_2R_G$, $-CN$, $-$
25 SCN , halogen, $-SR_G$, $-SOR_G$, $-SO_2R_G$, $-NO_2$, $-N(R_G)_2$, $-NHC(O)R_G$, or an aliphatic,
26 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently
27 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
28 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

29 wherein R_8 is hydrogen, alkyl, $-OH$, protected hydroxyl, $=O$, $-CN$, $-SCN$, halogen, $-SH$,
30 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

31 wherein m is 0-5;

1 wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, $-OR_H$, $=O$, $-C(=O)R_H$,

2 $-CO_2R_H$, $-CN$, $-SCN$, halogen, $-SR_H$, $-SOR_H$, $-SO_2R_H$, $-NO_2$, $-N(R_H)_2$, $-NHC(O)R_H$, or an
3 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
4 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
5 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

6 whereby if at least either X_1 and X_2 or X_3 and X_4 are doubly bonded to the 6-membered
7 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
8 and one double bond, and a quinone moiety is generated, or if at least either X_1 and X_2 or X_3 and
9 X_4 are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
10 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
11 generated;

12 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
13 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
14 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
15 unsubstituted; and pharmaceutically acceptable derivatives thereof; and

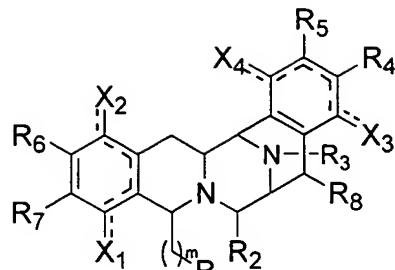
16 optionally further comprising a pharmaceutically acceptable carrier or diluent.

17
18 69. The method of claim 68, wherein said composition further comprises one or more
19 additional therapeutic agents.

20
21 70. The method of claim 69, wherein said composition further comprises one or more
22 cytotoxic agents.

23
24 71. The method of claim 68, wherein the cancer cells comprise melanoma cancer cells or
25 lung cancer cells.

26
27 72. A method for treating cancer comprising:
28 administering to a subject in need thereof a therapeutically effective amount of a
29 composition comprising a compound of formula (I) or pharmaceutically acceptable derivatives
30 thereof:



1
2 (I)
3

4 wherein R_1 is $NR_A R_B$, $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic,
5 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
6 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently
7 hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
8 moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or
9 cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-$
10 SR_D , $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
11 occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
12 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
13 moiety;

14 wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-$
15 SOR_E , $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
16 moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an
17 aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio,
18 heteroaryloxy, or heteroarylthio moiety;

19 wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an
20 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is
21 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
22 alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

23 wherein R_4 and R_6 are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl,
24 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

25 wherein R_5 and R_7 are each independently hydrogen, $-OR_G$, $-C(=O)R_G$, $-CO_2R_G$, $-CN$, $-$
26 SCN , halogen, $-SR_G$, $-SOR_G$, $-SO_2R_G$, $-NO_2$, $-N(R_G)_2$, $-NHC(O)R_G$, or an aliphatic,
27 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently

1 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
2 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

3 wherein R₈ is hydrogen, alkyl, -OH, protected hydroxyl, =O, -CN, -SCN, halogen, -SH,
4 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

5 wherein m is 0-5;

6 wherein X₁, X₂, X₃ and X₄ are each independently hydrogen, -OR_H, =O, -C(=O)R_H,
7 -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an
8 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
9 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
10 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

11 whereby if at least either X₁ and X₂ or X₃ and X₄ are doubly bonded to the 6-membered
12 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
13 and one double bond, and a quinone moiety is generated, or if at least either X₁ and X₂ or X₃ and
14 X₄ are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
15 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
16 generated;

17 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
18 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
19 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
20 unsubstituted; and

21 optionally further comprising a pharmaceutically acceptable carrier or diluent.

22

23 73. The method of claim 72, wherein said composition further comprises one or more
24 additional therapeutic agents.

25

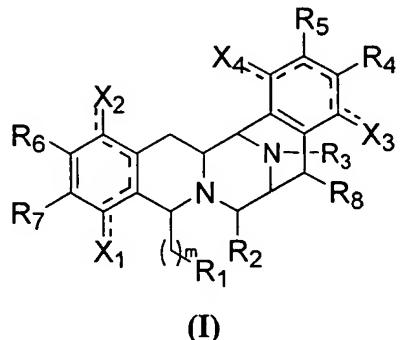
26 74. The method of claim 73, wherein said composition further comprises one or more
27 cytotoxic agents.

28

29 75. The method of claim 72, wherein the cancer cells comprise melanoma cancer cells or
30 lung cancer cells.

31

1 76. A method for the synthesis of a compound having the formula (I):



wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic, aliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or (aliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl group, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or heteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio group;

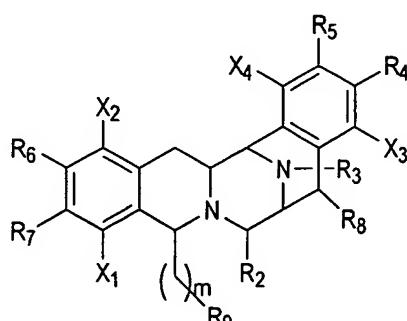
wherein R₂ is hydrogen, -OR_E, =O, -C(=O)R_E, -CO₂R_E, -CN, -SCN, halogen, -SR_E, -SO₂R_E, -NO₂, -N(R_E)₂, -NHC(O)R_E, or an aliphatic, heteroaliphatic, aryl, or heteroaryl group, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, aryloxy, or heteroarylthio moiety;

wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, α , aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R₄ and R₆ are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl, aryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

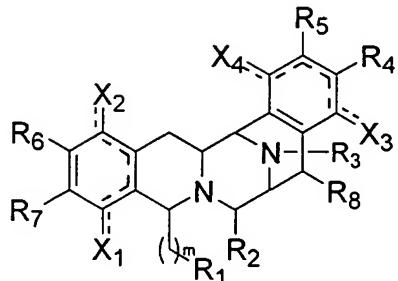
wherein R₅ and R₇ are each independently hydrogen, -OR_G, -C(=O)R_G, -CO₂R_G, -CN, -halogen, -SR_G, -SOR_G, -SO₂R_G, -NO₂, -N(R_G)₂, -NHC(O)R_G, or an aliphatic,

1 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently
2 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
3 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;
4 wherein R_8 is hydrogen, alkyl, -OH, protected hydroxyl, =O, -CN, -SCN, halogen, -SH,
5 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;
6 wherein m is 0-5;
7 wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, - OR_H , =O, -C(=O) R_H ,
8 -CO₂ R_H , -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂ R_H , -NO₂, -N(R_H)₂, -NHC(O) R_H , or an
9 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
10 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
11 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;
12 or wherein X_1 and R_7 taken together comprise a heterocyclic moiety;
13 whereby if at least either X_1 and X_2 or X_3 and X_4 are doubly bonded to the 6-membered
14 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
15 and one double bond, and a quinone moiety is generated, or if at least either X_1 and X_2 or X_3 and
16 X_4 are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
17 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
18 generated;
19 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
20 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
21 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
22 unsubstituted; wherein said method comprises:



(XV); and

(b) reacting said compound of formula (XV) under suitable conditions to generate a compound of formula (I):



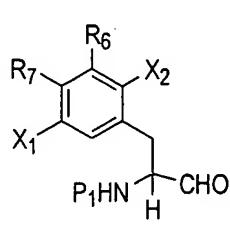
(1)

wherein X_1 - X_4 , R_1 - R_8 , and m are as described above and in classes and subclasses herein,

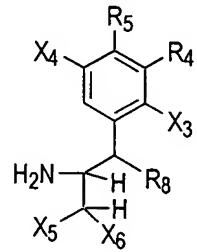
and

wherein the step of providing a compound of formula (XV) further comprises:

(1) reacting a first N-protected and a second C-protected α -amino aldehyde precursor having the structures:

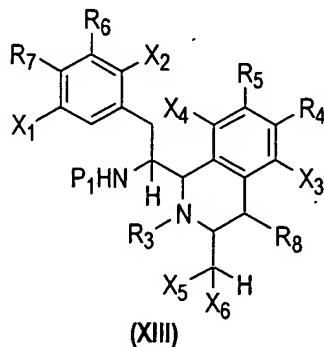


(XI)



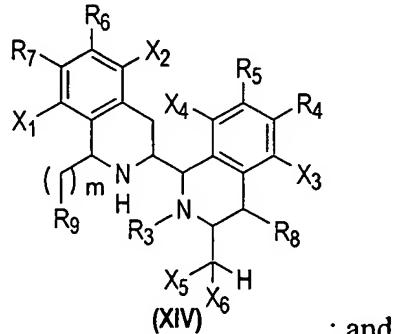
(XII)

under suitable conditions to generate a tetrahydroisoquinoline core having the structure (IX):



(2) optionally reacting said tetrahydroisoquinoline core under suitable conditions to diversify R_3 ;

(3) reacting a third aldehyde precursor having the structure: $R_9(CH_2)_mCHO$, with said tetrahydroisoquinoline core structure (**XIV**) under suitable conditions to generate a trimer of aldehydes having the structure:



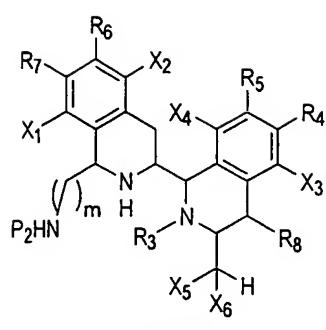
(4) reacting said trimer of aldehydes under suitable conditions to generate a compound of structure (XV),

wherein P₁ is hydrogen or a nitrogen protecting group;

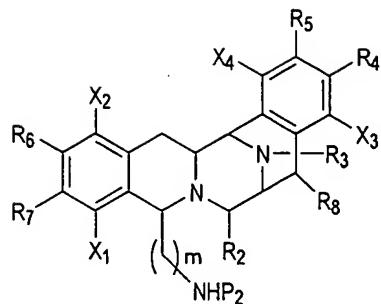
10 X₅ and X₆ taken together represent a carbon protecting group, optionally substituted with
11 a solid support unit; and

12 R₉ is NR_LR_M, -OR_L, -SR_L, -C(=O)R_L, -C(=S)R_L, -S(O)₂R_L, or an aliphatic,
13 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
14 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_L and R_M is independently
15 hydrogen, -(C=O)R_N, -NHR_N, -(SO₂)R_N, -OR_N, or an aliphatic, heteroaliphatic, aryl, or
16 heteroaryl moiety, or R_L and R_M, when taken together form an aryl, heteroaryl, cycloaliphatic, or
17 cycloheteroaliphatic moiety, wherein each occurrence of R_N is independently hydrogen, -OR_P, -
18 SR_P, -NHR_P, -(C=O)R_P, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
19 occurrence of R_P is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
20 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
21 moiety.

23 77. The method of claim 76, wherein for the intermediates **(XIV)** and **(XV)** R_9 is $-NHP_2$, P_2
24 is a nitrogen protecting group, and the intermediates have the structures **(XIVa)** and **(XVa)**:



1 (XIVa)



2 (XVa)

3 78. The method of claim 76, wherein $\text{R}_9(\text{CH}_2)_m\text{CHO}$ is (aliphatic)(C=O)(CH₂)_mCHO,
4 (heteroaliphatic)(C=O)(CH₂)_mCHO, (aliphatic)(CH₂)_mCHO, (heteroaliphatic)(CH₂)_mCHO,
5 aryl(aliphatic)(CH₂)_mCHO, aryl(heteroaliphatic)(CH₂)_mCHO, -heteroaryl(aliphatic)(CH₂)_mCHO,
6 or heteroaryl(heteroaliphatic)(CH₂)_mCHO,

7 wherein each of the aliphatic, and heteroaliphatic moieties is independently cyclic
8 or acyclic, linear or branched, or substituted or unsubstituted and wherein the aryl and
9 heteroaryl moieties are independently substituted or unsubstituted.

10
11 79. The method of claim 76, wherein $\text{R}_9(\text{CH}_2)_m\text{CHO}$ is $\text{CH}_3(\text{CH}_2)_{1-6}\text{CHO}$; (protecting
12 group) $\text{O}(\text{CH}_2)_{1-6}\text{CHO}$; (protecting group) $\text{NH}(\text{CH}_2)_{1-6}\text{CHO}$; (protecting group) $\text{S}(\text{CH}_2)_{1-6}\text{CHO}$;
13 (alkyl) $\text{O}(\text{C=O})\text{CHO}$; (aryl)(alkenyl) CHO ; (heteroaryl)(alkenyl) CHO ; (aryl) CHO ; or
14 (heteroaryl) CHO ,

15 wherein each of the aliphatic, and heteroaliphatic moieties is independently cyclic
16 or acyclic, linear or branched, or substituted or unsubstituted and wherein the aryl and
17 heteroaryl moieties are independently substituted or unsubstituted.

18
19 80. The method of claim 76, wherein X_5 is CN and X_6 is a heterocyclic moiety optionally
20 substituted with a solid support unit.

21
22 81. The method of claim 76, wherein the alkaloid structure (I) generated is that of saframycin
23 A.
24

1 82. The method of claim 76, wherein the method is stereoselective and the alkaloid structure
2 (I) generated is that of -(*-*) saframycin A.

3

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